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09/336,672	06/17/1999	MATTHIAS G. VON HERRATH	SCRIP1100	7934

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EXAMINER
SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
1636	24

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/336,672	Applicant(s) Von Herrath
	Examiner William Sandals	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 1, 2002*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *40, 41, 45, 46, 54, 55, 58-63, and 66-83* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *40, 41, 45, 46, 54, 55, 58-63, and 66-83* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Oct 1, 2002* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Amendments to the claims in Paper No.28, filed October 1, 2002 have overcome the rejection of the claims under 35 USC 112, second paragraph in the previous office action, and the rejection is withdrawn.

2. Amendments to the claims in Paper No.28 have overcome the rejection of the claims under 35 USC 102 in the previous office action, and the rejection is withdrawn.

3. Amendments to the claims in Paper No 28 have overcome the rejection of the claims under 35 USC 103 in the previous office action, and the rejection is withdrawn.

4. Applicant's arguments with respect to claims 40, 41, 45, 46, 54, 55, 58-60, 62, 63 and 66-68 have been considered but are moot in view of the new ground(s) of rejection. Responses to arguments which apply to the newly made instant rejections are included in the rejections below.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.**

Drawings

6. The drawings as submitted on October 1, 2002, have been approved by the draftsman.

Claim Objections

7. Claims 45, 46, 58, 66, 67, 71, 72, 74-77 and 81 are objected to because of the following informalities: Claims 44,71 and 74-77 are improperly dependent, either from a cancelled claim, a later numbered claim or to itself. It is assumed for the purposes of examination, that the above cited claims depend from their most proximal preceding independent claim. Claims 45, 58 and 66 all recite "operatively linked to nucleic acid" at line 2. The word "the" is omitted before "nucleic acid". Claims 46, 59, 67, 72, 76 and 81 all recite a Markush group of promoters, where the last 6 elements of the group do not recite the word "promoters". Claim 75 recites "element operatively to the nucleic acid" at line 2. The word "linked" has been omitted before "to the nucleic acid". Appropriate correction is required.

Claim Rejections - 35 USC § 112

8.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 62, 63 and 66-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 62 recites the limitation "the IL-10" in line 5. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 40, 41, 54, 55, 60-63, 68-70, 73, 74, 78 and 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,027,159 (Kaufman et al.) in view of US 5,891435 (Muir et al., of record).

The claims are drawn to immunomodulating compositions for treating a condition of an autoimmune process associated with autoimmune diabetes (Type I diabetes). The compositions comprise one or more nucleic acid constructs encoding GAD self-antigen and IL-10 in a pharmaceutically acceptable carrier, or the composition comprises one or more nucleic acid constructs encoding insulin-B self-antigen and IL-4 and/or IL-10 in a pharmaceutically acceptable carrier. The claims are also drawn to methods of treating a condition of an autoimmune process associated with autoimmune diabetes by peripherally administering the compositions to a subject and expressing the nucleic acid construct(s). The constructs may comprise operatively linked promoters (various). The method may comprise controlling the blood sugar of the subject. T-cells may be reactive to the GAD self-antigen.

Kaufman et al. teach at columns 2-5, 9-10 and the claims, compositions which may comprise GAD self-antigen or insulin-B self-antigen and IL-4 and/or IL-10 (see for example

column 3, lines 1-10, and lines 46-55) in a pharmaceutically acceptable carrier. Kaufman et al. teach methods of treating a condition of an autoimmune process associated with autoimmune diabetes by peripherally administering the compositions to a subject, thereby controlling the blood sugar of the subject (see especially column 4, lines 27-35, for example). T-cells may be reactive to the GAD self-antigen.

Kaufman et al. did not teach the administration of the self-antigens via nucleic acids encoding the self-antigens, and interleukins.

Muir et al. teach at columns 5-7, 9 and example 4, immunomodulating compositions for treating a condition of autoimmune process associated with autoimmune diabetes (Type I diabetes). The compositions comprise one or more nucleic acid constructs (viral vectors) encoding GAD self-antigen or insulin-B self-antigen (see especially column 5, lines 4-14, for example) in a pharmaceutically acceptable carrier. The claims are also drawn to methods of treating a condition of autoimmune process associated with autoimmune diabetes by peripherally administering the compositions to a subject and expressing the nucleic acid construct(s) (see column 5, lines 39-52, for example). Muir et al. discuss the use of IL-10 as a costimulatory antigen, which may be useful in the method, at column 9, lines 29-53. The constructs may comprise operatively linked promoters. The method may comprise controlling the blood sugar of the subject. Muir et al. discuss the advantageous use of nucleic acid immunization for prolonged immunostimulation of the subject at Example 4.

It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of Muir et al. with the teachings of Kaufman et al. because Both Kaufman et al. and Muir et al. teach the immunization of a subject with either GAD self-antigen or insulin-B self antigen making obvious the composition comprising a nucleic acid construct to immunize a subject in a method of treating autoimmune diabetes with either GAD self-antigen or insulin-B self antigen. Thus it is prima facie obvious to produce a composition comprising a nucleic acid construct to immunize a subject in a method of treating autoimmune diabetes with either GAD self-antigen or insulin-B self antigen with the additional teachings of Muir et al. that it is advantageous and desirable to use a nucleic acid (viral vector) to introduce a construct encoding either GAD self-antigen or insulin-B self-antigen for prolonged immunostimulation of the subject.

One of ordinary skill in the art would have been motivated to combine the teachings of Muir et al. with the teachings of Kaufman et al. to produce a composition comprising a nucleic acid construct to immunize a subject in a method of treating autoimmune diabetes with either GAD self-antigen or insulin-B self antigen because both Kaufman et al. and Muir et al. teach the immunization of a subject with either GAD self-antigen or insulin-B self antigen where Muir et al. teach the advantageous and desirable use of a nucleic acid (viral vector) to introduce a construct encoding either GAD self-antigen or insulin-B self antigen for prolonged immunostimulation of the subject. Further, a person of ordinary skill in the art would have had a

reasonable expectation of success in the producing the instant claimed invention given the teachings of Muir et al. and Kaufman et al.

13. Claims 40, 41, 45, 46, 54, 55, 58-63 and 66-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muir et al. with Kaufman et al. as applied to claims 40, 41, 54, 55, 60-63, 68-70, 73, 74, 78 and 79 above, and further in view of US 6,313,272 (Greve et al.).

The claims are as described above and also where the nucleic acid construct is operatively linked to a regulatory element which may be a promoter (various).

Muir et al. and Kaufman et al. teach the invention as described above.

Muir et al. and Kaufman et al. did not teach that the nucleic acid construct is operatively linked to a regulatory element which may be a promoter (various).

Greve et al. teach at columns 2 (especially lines 35-53) and 6 (especially lines 36-54) the advantageous use of nucleic acid constructs operably linked to various promoters to regulate the expression of IL-4 in a method of treating autoimmune diabetes. Greve et al. teach that the promoter choice is within the purview of the ordinary skilled artisan and may be predicated upon the host/vector system being employed.

It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of Muir et al. and Kaufman et al. with Greve et al. because Muir et al., Kaufman et al. and Greve et al. teach a composition comprising a nucleic acid construct which is used in a method to immunize a subject for treating autoimmune diabetes

making prima facie obvious the additional teachings of Greve et al. of various operably linked promoters which are useful in controlling the expression of the encoded antigen composition in the composition and methods for treating autoimmune diabetes of Muir et al. and Kaufman et al.

One of ordinary skill in the art would have been motivated to combine the teachings of Muir et al. and Kaufman et al. with Greve et al. to produce a composition comprising a nucleic acid construct to immunize a subject in a method of treating autoimmune diabetes because each of Kaufman et al., Muir et al. and Greve et al. teach the immunization of a subject with a nucleic acid construct encoding an antigen for immunostimulation of the subject to treat autoimmune diabetes where Greve et al. teach desirable and useful operably linked promoters which are choices within the purview of the ordinary skilled artisan. The promoter choice may be predicated upon the host/vector system being employed. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Muir et al. and Kaufman et al. with Greve et al.

14. Claims 40, 41, 45, 46, 54, 55, 58-63 and 66-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muir et al., Kaufman et al. and US 6,313,272 (Greve et al.) as applied to claims 40, 41, 45, 46, 54, 55, 58-63 and 66-82 above, and further in view of US 5,951,976 (Segal).

The claims are as described above and also where the nucleic acid construct is naked DNA.

Muir et al. and Kaufman et al. with Greve et al. teach the invention as described above.

Muir et al. and Kaufman et al. with Greve et al. did not teach that the nucleic acid construct is naked DNA.

Segal teaches at columns 3-6 and 17-18 the advantageous expression of nucleic acids, which may be naked nucleic acids, which may encode a GAD self-antigen (see column 18, lines 13-28, for example) and interleukins 4 and 10 (see column 4, lines 30-34, for example) in a method of treating autoimmune diabetes where naked DNA is useful in a method of introduction of the nucleic acid into cells of a subject for expression of the nucleic acid construct in the method of treatment (see column 18, line 51 to column 22, line 19, for example).

It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of Muir et al., Kaufman et al. and Greve et al. with Segal because each of Muir et al., Kaufman et al., Greve et al. and Segal teach the immunostimulation of a subject to treat autoimmune diabetes with a nucleic acid construct encoding an antigen making obvious the additional teachings of Segal that the useful and desirable expression of naked nucleic acids encoding an antigen which may be GAD, and interleukins 4 and 10 which is useful in the method of treating autoimmune diabetes of Muir et al. and Kaufman et al. and Greve et al.

One of ordinary skill in the art would have been motivated to combine the teachings of Muir et al. and Kaufman et al. and Greve et al. with Segal to produce a composition comprising a nucleic acid construct to immunize a subject in a method of treating autoimmune diabetes

because each of Muir et al. and Kaufman et al., Greve et al. and Segal teach the immunostimulation of the subject to treat autoimmune diabetes with a nucleic acid construct encoding an antigen for immunostimulation of the subject and Segal teaches the desirable and beneficial use of a naked DNA in a method of introduction of the composition comprising the nucleic acid construct into cells of a subject for expression of the nucleic acid construct in the method of treatment. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Muir et al. and Kaufman et al. and Greve et al. with Segal.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the William Phillips, whose telephone number is (703) 305-3482.

William Sandals, Ph.D.
Examiner
December 9, 2002

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
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